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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/782,075	02/19/2004	Sean D. Monahan	25772 US2	4417
83890	7590	02/18/2010		
ROCHE MADISON INC. 465 Science Drive Suite C MADISON, WI 53711			EXAMINER CHONG, KIMBERLY	
			ART UNIT 1635	PAPER NUMBER
			MAIL DATE 02/18/2010	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/782,075

**Applicant(s)**

MONAHAN ET AL.

**Examiner**

KIMBERLY CHONG

**Art Unit**

1635

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 27 January 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 4-6, 10, 13 and 14 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 4-6, 10, 13, 14 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/S508)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Request for Continued Examination***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/27/2010 has been entered.

### ***Status of Application/Amendment/Claims***

Applicant's response 01/27/2010 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 11/05/2009 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 01/27/2010, claims 1, 4-6, 10, 13 and 14 are pending in the application.

### ***Response to Applicant's Arguments***

#### ***Claim Rejections - 35 USC § 112 - withdrawn***

The rejection of claims 1, 4-6, 10, 13 and 14 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn as

a review of the instant specification provides support for the term "reversibly modified" on page 5 line 21.

The rejection of claims 1, 4-6, 10, 13 and 14 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn due to claim amendments.

***Claim Rejections - 35 USC § 102 - maintained***

The rejection of claims 1, 5, 6, 10 and 13-14 under 35 U.S.C. 102(e) as being anticipated by Fosnaugh et al. (US 2003/0143732 of record PTO Form 892 mailed 12/31/2007) as evidenced by Thierry et al. (US 6,110,490) is maintained for the reasons of record.

Applicant's arguments filed 01/27/2010 have been fully considered but they are not persuasive. Applicant argues Fosnaugh et al. do not provide any motivation or desire for the specific combination of a lipid-siRNA with a cationic lipid and cites case law that involve decisions over whether there is a prima facie case of obviousness. Fosnaugh et al. is used in a 102 rejection and therefore does not need to provide any motivation or desire for a specific combination of lipid-siRNA. Fosnaugh et al. only need to teach the claimed limitations. Applicant argues Fosnaugh et al. do not teach the RNA conjugated to a lipid via a labile bond cleavable under mammalian conditions. As stated previously, Fosnaugh et al. teach the siRNA can be modified at the 2' hydroxyl position

and teach the functional groups are attached to the siRNA via biodegradable linkers wherein the linkers are degradable in biological systems i.e. mammalian cells which would meet the limitations of cleavable under mammalian conditions.

Applicants next argue Thierry et al do not teach the association of the nucleic acid with a liposome is enhanced by a hydrophobic interaction between the two. This new claim limitation reciting "wherein association of the RNA to the transfection reagent is *enhanced* via hydrophobic interactions between the hydrophobic group linked to the RNA..." has been discussed in the previous Office action filed 12/10/2008 wherein the subsequent claim amendments filed 03/09/2009 removed this limitation. In the previous Office action the limitation of enhancing the interaction of the siRNA to the transfection reagent was interpreted very broadly because the instant specification does not define what "enhances the interaction" of a siRNA with a transfection reagent. Page 3, lines 26-32 which states:

"In a preferred embodiment, we describe methods to alter the interaction of an siRNA with a cell or transfection agent comprising: reacting the siRNA with a modifying agent wherein the modifying agent contains a hydrophobic group. The transfection agent can comprise polymers, lipids, detergents, or surfactants, or a combination of polymers, lipids, detergents, or surfactants. Hydrophobic modification of the siRNA allows hydrophobic interaction of the siRNA with the transfection agent."

The instant specification does not describe which hydrophobic groups enhance the interaction of the siRNA with a transfection agent and does not describe what encompasses the term "enhances". The term enhances is interpreted to mean any interaction of a siRNA molecule comprising a hydrophobic group with a transfection agent such that the siRNA is capable of entering a cell. Based on the description of a

hydrophobic modification of an siRNA from the specification and interpretation of the claim limitations, a siRNA which consists of any hydrophobic modification would allow interaction of the siRNA with the transfection agent and therefore would alter i.e. enhance the interaction of a siRNA with a transfection agent.

Thus because Fosnaugh et al. teach conjugates comprising siRNA and functional groups that are complexed with liposomes and because Thierry et al. teach liposomal complexes comprising oligonucleotides are formed by hydrophobic interactions, Fosnaugh et al. anticipates the instant claims and the rejection is maintained.

The rejection of claims 1, 5, 6, 10 and 13-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Lewis et al. (US 2003/0143204 of record PTO Form 892 mailed 12/31/2007) and further evidenced by Thierry et al. (US 6,110,490) is maintained for the reasons of record.

Applicant clarifies a previous argument and states that Lewis et al. do not teach that a functional group can be attached to an RNA via a labile bond and further maintains that Lewis et al. do not teach that the functional group can be a hydrophobic group.

As stated in the previous action, Lewis et al. teach the RNA compounds are attached to one or more functional groups wherein such functional groups are cell targeting compounds, carbohydrates and lipids which are hydrophobic. Lewis et al. beginning at paragraph 0120, Lewis et al. discuss the use of labile bonds for attachment

of polymers and lipids and teach said functional groups are attached via said labile bonds that can be selectively broken and dissociated to provide an active inhibitor in the cell.

Thus Lewis et al. anticipates the instant claims and the rejection is maintained.

***Claim Rejections - 35 USC § 103 - maintained***

The rejection of claims 1, 4-6, 10, 13 and 14 under 35 U.S.C. 103(a) as being obvious over Fosnaugh et al. (US 2003/0143732 of record PTO Form 892 mailed 12/31/2007), Manoharan, M. (Biochimica et Biophysica Acta 1489, 1999: 117-130 of record PTO Form 892 mailed 12/31/2007) and further evidenced by Thierry et al. (US 6,110,490) is maintained for the reasons of record.

Applicant states that the amendments and arguments made above in the response to the 102 rejection are sufficient to overcome the 103 rejections. Response to Applicant's arguments are addressed above and do not overcome the 102 rejections of record and therefore do not overcome the 103 rejection.

Thus, the rejection of record is maintained.

The rejection of claims 1, 4-6, 10, 13 and 14 under 35 U.S.C. 103(a) as being obvious over Lewis et al. (US 2003/0143204 of record PTO Form 892 mailed 12/31/2007), Manoharan, M. (Biochimica et Biophysica Acta 1489, 1999: 117-130 of record PTO Form 892 mailed 12/31/2007) and further evidenced by Thierry et al. (US 6,110,490) is maintained for the reasons of record.

Applicant states that the amendments and arguments made above in the response to the 102 rejection are sufficient to overcome the 103 rejections. Response to Applicant's arguments are addressed above and do not overcome the 102 rejections of record and therefore do not overcome the 103 rejection.

Thus, the rejection of record is maintained.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful please contact Tracy Vivimore at 571-272-2914. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Kimberly Chong/  
Primary Examiner  
Art Unit 1635